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Dockets Management Branch (HFA-325)
Food and Drug Administration
Department of Health and Human Services
12420 Parklawn Drive, Room 1-23
Rockville, MD 20857

**THIRD AMENDED CITIZEN PETITION**

The undersigned submits this Amended Petition under Section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)(2)(C)), which authority has been delegated to the Commissioner of Food and Drugs under 21 C.F.R. § 5.1. The original Petition, assigned Docket No. 98P-1219/CP1, was submitted December 21, 1998. Petitioner requests the Commissioner of Food and Drugs to make a determination that the drug products hereinafter described are suitable for consideration in an abbreviated new drug application (ANDA).

## A. Action Requested

King & Spalding requests a determination that drug products containing either 4.5 mg oxycodone hydrochloride and 0.38 mg oxycodone or 2.25 mg oxycodone hydrochloride and 0.19 mg oxycodone terephthalate, and 325 mg acetaminophen in a tablet for oral administration are suitable for evaluation under an ANDA.

## B. Statement of Grounds

The reference listed drugs upon which this petition is based are Endo Pharmaceuticals' Percodan tablets (# N07337 006, Approved Drug Products with Therapeutic Equivalence Evaluations 18th Edition ("The Orange Book"), p. 3-33) containing oxycodone hydrochloride 4.5 mg/oxycodone terephthalate 0.38 mg/aspirin 325 mg and Percodan Demi tablets (# N07337 005, The Orange Book, p. 3-33) containing oxycodone hydrochloride 2.25 mg/oxycodone terephthalate 0.19 mg/aspirin 325 mg.

The adult and pediatric dosing of the reference listed drugs are shown in the enclosed package insert (Attachment 1). The strengths and dosing of the proposed combination products will be the same as the reference listed drugs. The maximum daily dose of acetaminophen based

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on the recommended dosing of one to two tablets every six hours will be 2600 mg, which is well within the generally recognized safe limit of 4000 mg/day. A side by side comparison of the reference and proposed package insert is enclosed as Attachment 2.

The proposed products are similar to the reference products, Percodan and Percodan Demi, in that one product contains 4.5 mg oxycodone hydrochloride and 0.38 mg oxycodone terephthalate and the other product contains 2.25 mg oxycodone hydrochloride and 0.19 mg oxycodone terephthalate. The proposed products differ from the reference products in that 325 mg acetaminophen (APAP) is substituted for 325 mg aspirin (ASA).

According to the Tentative Final Monograph for OTC Internal Analgesic, Antipyretic, and Antirheumatic Products (53 Fed. Reg. 46204 (Nov. 16,1988)), the analgesic efficacy of APAP is equal to that of ASA:

> The agency believes at this time that it is reasonable for acetaminophen and aspirin to have the same dosage and frequency of administration because, based upon the data submitted to the Panel, the safe and effective OTC dosage ranges for acetaminophen and aspirin are the same -- 325 mg to 650 mg every 4 hours, not to exceed 4 g in 24 hours. Also, aspirin and acetaminophen are indicated for the same OTC uses, have been extensively promoted as comparable OTC analgesics (with different side effects), and are widely and interchangeably used by consumers.

53 Fed. Reg. at 46236. Thus, the proposed products' 325 mg APAP is pharmacologically equivalent to the reference products' 325 mg ASA.

Furthermore, the agency has previously approved petitions (no ANDAs filed) substituting equipotent doses of ASA and APAP (Attachment 3). The petition approvals include several products with equipotent doses (ranging from 325 mg - 650 mg) of ASA and APAP in combination with the opioids hydrocodone bitartrate or dihydrocodeine bitartrate. There are also several approved combination products containing active ingredients that are the same similar except for equipotent doses of acetaminophen or aspirin (Attachment 4).

### C. Environmental Impact

As provided in 21 C.F.R. 25.31, neither an environmental assessment nor an environmental impact statement is required.

**D. Economic Impact**

As provided in 21 C.F.R. 10.30(b), economic impact information is to be submitted only when requested by the Commissioner following review of the petition.

**E. Certification**

The undersigned certifies that to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to us which are unfavorable to the petition.

Sincerely,

KING & SPALDING

By: _____
Jess H. Stribling

Attachments